

The University of Chicago

THE ISOMERIZATION
OF CIS-TRANS ETHYLENE ISOMERS
BY HALOGEN ACIDS

A DISSERTATION SUBMITTED TO THE FACULTY
OF THE DIVISION OF THE PHYSICAL SCIENCES
IN CANDIDACY FOR THE DEGREE OF DOCTOR
OF PHILOSOPHY

DEPARTMENT OF CHEMISTRY
JUNE, 1942

By
J. VICTOR MANSFIELD

CHICAGO, ILLINOIS
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INTRODUCTION

For some years now, an extensive investigation of the addition of halogen acids to ethylenic compounds has been under way in this laboratory. Naturally, before long, the important question arose concerning the mechanism of the addition. This question had even more significance in reference to ethylenic compounds, which were capable of existing in malenoid (cis) and fumaroid (trans) modifications, since here the question of addition to the malenoid or fumaroid isomer became paramount, because the addendum reagent (halogen acid) had the property of isomerizing the malenoid to the fumaroid form. It soon became evident that the problem of the addition of halogen acids to cis-trans ethylenic isomers had two distinct aspects. First, are all malenoid (cis) compounds first transformed into their fumaroid (trans) modification by halogen acids, so that addition is always to the fumaroid form? Second, do halogen acids add in a cis or trans manner to the ethylenic compound?

Kharasch¹ and co-workers have shown in numerous instances that unsaturated derivatives of the type $R_1CH:CHR_2$ add halogen acids very rapidly when R_1 and R_2 are aliphatic radicals. In fact, the addition is so fast that it has been impossible to determine which isomer adds the halogen acid more rapidly; or whether there is any isomerization of the malenoid to the fumaroid form, either previous to, or during the addition reaction. In order to study the mechanism of the addition of halogen acids to cis-trans ethylenic compounds, it was decided to work with derivatives in which R_1 and R_2 were aromatic groups, since it has been shown in this laboratory² that p-chlorocisostilbene adds halogen acids relatively slowly in dilute benzene solution. This relatively slow addition of halogen acid permits a study of not only the addition reaction, but also the isomerization process.

¹Kharasch, Darkis, Mayo, Hinckley, Walling, unpublished work.

²M. A. Bloodgood, Doctor's Dissertation, University of Chicago (1931).

It was thought that by choosing the radicals R_1 and R_2 judiciously, a series of compounds could be prepared which would enable one to make a detailed investigation of the interesting and important questions raised in the foregoing discussion.

It was decided to prepare isostilbene and α -phenylcinnamic acid (labile form), and investigate exhaustively the factors influencing their isomerization by halogen acids. Furthermore, maleic acid and dimethyl maleate were also prepared and studied in an effort to elucidate the isomerization process. In the case of the first two compounds mentioned (isostilbene and α -phenylcinnamic acid (labile)), an amazing difference in the rate of isomerization was observed when the process was carried out with hydrogen bromide and added peroxides, and when it was carried out with hydrogen chloride. In the presence of hydrogen bromide and peroxides, the isomerization was complete in less than two minutes, whereas in the presence of hydrogen chloride at least six days for isostilbene and eleven days for α -phenylcinnamic acid (labile) were necessary to effect isomerization. The other compounds, namely, maleic acid and dimethyl maleate, exhibited no such marked difference in their rate of isomerization by means of hydrogen chloride and hydrogen bromide. It appeared that both halogen acids were equally effective in causing their isomerization.

Apparently, in the case of aromatic derivatives, we are dealing with two entirely distinct mechanisms of isomerization: the extremely rapid "peroxide catalyzed" isomerization with hydrogen bromide, for which a bromine atom mechanism is proposed, and a much slower isomerization by the aid of hydrogen chloride. In the case of the aliphatic derivatives, however, the results lead one to believe that the isomerization is effected by an ionic mechanism, involving hydrogen ions or halogen ions.

As mentioned before, a very important phase of this investigation was concerned with the question whether the addition of the halogen acid occurs cis or trans to the ethylenic derivative. It would be a meaningless question to ask whether such compounds as isostilbene, maleic acid, etc., add halogen acid in a cis or in a trans manner, since the final addition product would be the same in either case. To answer this important question, it is necessary to select compounds which after addition contain two asymmetric carbon atoms, and are capable of existing

in a racemic and a meso form. The most convenient compounds to use appeared to be bromomaleic and bromofumaric acids, since the addition of halogen acids in this case would give rise, depending on whether the addition were "cis" or "trans," to two products (meso dihalogen succinic acid, and racemic dihalogen succinic acid) both of which are well characterized and easily separable from each other.

The addition of hydrogen bromide to bromomaleic acid in various organic solvents was so rapid that the isomerization, which might have conceivably occurred first, was not observed. It is, however, a question whether isomerization would have occurred first if the addition were not so fast, for in the case of chloromaleic acid, where the addition of hydrogen chloride is quite slow, no isomerization was ever observed.

The reaction involving the addition of halogen acids to bromomaleic and bromofumaric acid is peculiar in that the addition products formed (meso and racemic dihalogen succinic acids) are the abnormal addition products. According to all the theories thus far formulated for the directed addition of halogen acids to double bonds, it would be expected that the 1, 1-dihalogen succinic acid would be formed. This directed addition of halogen acid to the double bond takes place in the normal manner in the case of citraconic and mesaconic acids, which were also studied in an effort to learn something about the factors involved in the isomerization process.

It was found in the case of citraconic acid (cis) that, when insufficient hydrogen bromide was employed to combine completely with the citraconic acid, a transformation of the citraconic acid (cis) to mesaconic (trans) occurred. In similar experiments with bromomaleic acid, supporting, but not conclusive, evidence was obtained that isomerization took place previous to addition. If this is true, there is reason to believe that in all cases where addition is carried out in air, isomerization of the malenoid (cis) to the fumaroid (trans) form would occur previous to the addition; and only in those cases where the addition is extremely fast would the addition be exclusively to the malenoid form. An ionic mechanism is advanced to explain the effect of less than molar equivalents of halogen acids in isomerizing the malenoid to fumaroid compound.

A summary of the literature on the addition of halogen

acids to cis and trans compounds of definitely established constitution is presented in Table 1. A cursory survey of these data reveals that most of the work done on the addition of halogen acids to cis and trans ethylenic compounds was not done in a very systematic or exhaustive manner. It will be observed that only ethylenic acids have been used in the past. The fact that the ethylenic acids exist in definitely established cis and trans forms probably accounts for their wide use in previous studies of this kind. It is evident from the literature that when addition occurs in the presence of air isomerization may take place in many cases previous to addition. The two exceptions which were found in the present work were: (1) the exceedingly rapid addition of hydrogen bromide to bromomaleic acid, which excludes previous isomerization; (2) under anti-oxidant conditions, the rate of isomerization of such compounds as isostilbene and α -phenylcinnamic acid (labile) is completely prevented, so that addition occurs directly to the malenoid form.

TABLE 1

A REVIEW OF THE LITERATURE ON THE ADDITION OF HALOGEN
ACIDS TO CIS-TRANS UNSATURATED ACIDS

Ethyleneic Acid	Reagent	Temp.	Reaction Time	Products Formed (Acids)	Reference
Maleic	HCl (aq. sat. at 0°)	18°	4 days	Fumaric, chlorosuccinic	3
Maleic	HI (aq.)	18°	1 day	Fumaric, succinic (?)	3
Maleic	HBr (aq. sat. at 0°)	18°		Fumaric	4
Maleic	HBr (aq.)	100°		Fumaric, bromosuccinic	4
Fumaric	HI in acetic acid (sat. at 0°)	100°	Few hrs.	Succinic	3
Fumaric	HCl (in acetic acid, sat. at 0°)	100°	12-14 hrs.	Chlorosuccinic	5
Fumaric	HBr (in acetic acid, sat. at 0°)	100°	2 hrs.	Bromosuccinic	5
Fumaric	HBr (fuming, aq.)	100°	12 hrs.	Bromosuccinic	6
Citraconic	HBr (aq.)	18°	4-5 days	Citrobromopyrotartaric	7
Citraconic	HCl (fuming, aq.)	18°	5 days	Mesochloropyrotartaric	7
Citraconic anhydride	HCl (aq. sat. at 0°)	120°	Few hrs.	Largely mesaconic, small amt. of a chlorinated acid	8
Mesaconic	HCl (conc. aq.)	140°		Mesochloropyrotartaric	9
Mesaconic	HBr (fuming, aq.)	140°		Some mesaconic recovered	10
Erucic	HBr (in acetic acid)	..		Mesobromopyrotartaric	11
Erucic	HI (aq.)	100°		μ or ν bromobehenic	12
Brassicic	HBr	..		Brassicic	13
Oleic and Elaidic	HCl (in acetic acid, sat. at 0°)	18°	3-4 days	Moniodobehenic	14
Oleic and Elaidic	HBr (in acetic acid, sat. at 0°)	18°	3-4 days	Monobromobehenic	14
Bromomaleic	HBr (fuming, aq.)	..		Monochlorostearic	15
Bromomaleic	HBr or HCl (dil., aq.)	Boiled	2 hrs.	Monobromostearic	16
Bromomaleic	HBr (fuming, aq.)	Cold	"Short"	Dibromosuccinic Racemic-dibromosuccinic Bromofumaric or chloro- fumaric Dibromosuccinic, bromo- fumaric	17

TABLE 1--Continued

Ethylenic Acid	Reagent	Temp.	Reaction Time	Products Formed (Acids)	Reference
Bromofumaric	HBr (fuming, aq.)	100°	"Short"	Dibromosuccinic	17
Bromofumaric	HBr (fuming, aq.)	Cold	"Long"	Racemic-dibromosuccinic	17
Isocrotonic	HI (aq.)	100°	Faster	Dibromosuccinic	18
Isocrotonic	HCl (gas)	18°		Racemic-dibromosuccinic	19
Isocrotonic	HBr (fuming, aq.)	100°		β -iodobutyric	20
Crotonic	HBr	18°	Few days	Crotonic	20
Crotonic	HCl (aq. sat. at 0°)	18°		α - and β -bromobutyric	21
Angelica	HBr (aq. sat. at 0°)	18°		β -bromobutyric	21
Angelica	HI (aq. sat. at 0°)	18°	5 days	β -chlorobutyric	22
Tiglic	HBr (aq. sat. at 0°)	18°	Few hrs.	Bromotiglic	22
Tiglic	HI (in chloroform)	0°	5 days	Hydroiodoangelic	22
Isocinnamic	HBr (aq.)	..	7 days	Hydroiodotiglic	24
Isocinnamic	HCl (aq.)	..	24 hrs.	β -bromohydrocinnamic	25
Cinnamic	HBr (sat. in acetic acid)	100°	"Short"	β -chlorohydrocinnamic	25, 26
Cinnamic	HBr (aq. sat. at 0°)	18°	2 days	Bromohydrocinnamic	27
Cinnamic	HI (aq. sat. at 0°)	18°	2 days	Bromohydrocinnamic	28
Cinnamic	HCl (aq. sat. at 0°)	18°	3 days	Iodohydrocinnamic	28
Cinnamic	HBr (aq. sat. at 0°)	18°	3 days	β -chlorohydrocinnamic	25
Cinnamic	HBr (aq. sat. at 0°)	18°	3 days	β -bromohydrocinnamic	25

References (Table 1)

- ³Skraup, Monatsh., 12, 120 (1891).
- ⁴Fittig, Ann., 188, 91 (1877).
- ⁵Anschutz and Bennert, Ber., 15, 642 (1882).
- ⁶Fittig and Dorn, Ann., 188, 88 (1877).
- ⁷Fittig, ibid., 188, 77 (1877).
- ⁸Fittig and Landolt, ibid., 188, 83 (1877).
- ⁹Fittig, ibid., 188, 51 (1877).
- ¹⁰Fittig, ibid., 188, 82 (1877); Swarts, Zeit. fur Chemie, 724 (1866).
- ¹¹Ponizio, Gazz. chim. ital., 35, II, 396 (1905).
- ¹²Alexandroff and Saytzeff, J. prakt. Chem. [2], 49, 58 (1894).
- ¹³Chem. Zentr., 1908, I, 2019.
- ¹⁴Piotrowski, Ber., 23, 2532 (1890).
- ¹⁵Fittig and Petri, Ann., 195, 77 (1879).
- ¹⁶Michael, J. prakt. Chem. [2], 52, 301 (1895).
- ¹⁷Anschutz, Ber., 10, 1885 (1877).
- ¹⁸Michael and Freer, J. prakt. Chem. [2], 40, 95 (1889).
- ¹⁹Wislicensus, Ann., 248, 341 (1888).
- ²⁰Fittig and Alberti, Ber., 9, 1194 (1876).
- ²¹Lovén and Johansen, Ber., 48, 1256 (1915).
- ²²Fittig and Pagenstecker, Ann., 195, 109, 111, (1879).
- ²³Schmidt, ibid., 208, 254 (1881).
- ²⁴Wislicensus and Talbot, ibid., 313, 231 (1900).
- ²⁵Liebermann, Ber., 23, 152 (1890).
- ²⁶Erlenmeyer, ibid., 14, 1867 (1881).
- ²⁷Anschutz and Kinnkutt, ibid., 11, 1221 (1878).
- ²⁸Fittig and Binder, Ann., 195, 132 (1879).

REVIEW OF THEORIES OF TRANSFORMATION OF
CIS TO TRANS CLASSES OF UNSATURATED
ETHYLENIC COMPOUNDS

Light is very often effective in causing an isomerization of cis-ethylenic compounds to their trans forms. In many cases the transformation remains incomplete in that a true equilibrium mixture is obtained. This equilibrium may be approached by starting with the malenoid or fumaroid form. For example B. C. Warburg²⁹ found by illuminating maleic and fumaric acid with ultraviolet the following equilibrium:



In a 0.00306 normal solution it was found that the following equilibria expressed in per cent of maleic acid occurred when the solution was exposed to light of different wave lengths.

$$\lambda = 207 \text{ m } \mu \text{ --- } 68.3\%$$

$$\lambda = 253 \text{ m } \mu \text{ --- } 63.5\%$$

$$\lambda = 282 \text{ m } \mu \text{ --- } 76.0\%$$

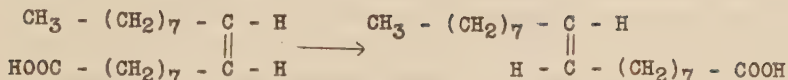
Iodine, especially in sunlight, is an effective catalyst for the isomerization of cis compounds to their trans form. The conversion of maleic acid esters to fumaric acid esters by means of potassium in ether has been reported by H. Meerwein.³⁰ W. Schlenk and E. Bergmann³¹ observed that isostilbene was isomerized to stilbene by metallic sodium. According to a very old procedure of Poutet (1819) nitrous acid is very effective in converting

²⁹Warburg, Ber. Berl. Akad., 1919, 960.

³⁰Meerwein, Ber., 58, 1266 (1926).

³¹Schlenk and Bergmann, Ann., 463, 110 (1928).

oleic acid to elaidic acid.

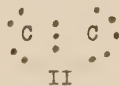
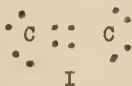


The conversion of many of the higher (*cis*) fatty acids containing a double bond may also be brought about by iodine, sulfur and through ultraviolet light. Many ethylenic compounds are isomerized by mineral acids. Halogen acids and nitric acid are very effective isomerizing agents.

In many cases the conversion is not caused by the catalyst which is added but by a product formed from this added compound. The conversion of erucic acid to brassidic acid by heating to 180° with NaHSO₃³² has been explained by A. Rankoff³³ as being due to the colloidal sulfur which is formed during the experiment. Also along the same line, the isomerization of citraconic acid to mesaconic acid by the action of concentrated hydrogen iodide solution may be due not to the reagent but actually to the trace of iodine present.

H. Freundlich and G. Schikorr³⁴ and Zd. H. Skraup³⁵ have found that colloidal sulfur is effective in converting maleic acid into fumaric acid.

A hypothesis has been advanced by R. Kuhn³⁶ for the isomerization of unsaturated ethylenic compounds which seems to explain in a rather satisfactory manner a large number of experimental data. He assumes that an ethylenic compound may exist in two valence tautomers.



³²C. M. and A. Saytzeff, J. prakt. Chem. [2], 50, 85 (1894).

³³Rankoff, Ber., 63, 2139 (1930).

³⁴Freundlich and Schikorr, Koll. Beih., 22, 1 (1926).

³⁵Skraup, Monatsh., 12, 108 (1891).

³⁶R. Kuhn in text of K. Freudenberg, "Stereochemie," Franz Deuticke, Leipzig und Wien, 1933, pp. 916 ff.

exhibit a greater freedom of rotation around the double bond than in its normal state. This therefore explains the catalytic effect of the isomerization of malenoid compounds by paramagnetic substances.

Since all paramagnetic compounds do not react with other paramagnetic compounds it is to be assumed that not all paramagnetic agents are capable of activating the ethylenic double bond. Likewise a loosening of the double bond by the action of diamagnetic catalysts may occur when the charge on the catalyst (hydrogen ion, highly charged cations, etc.) exerts a marked polarizing effect on the double bond and in this way causes a loosening or electron displacement in ethylenic compounds. The cis-trans isomerization by means of diamagnetic substances such as hydrogen chloride may be explained in this fashion.

FACTORS INFLUENCING TRANSFORMATION
OF CIS TO TRANS ISOMERS

a. Isostilbene

A thorough investigation of the isomerization of isostilbene revealed that this transformation by means of hydrogen bromide in solvents (benzene and dioxane) is markedly accelerated by (a) peroxides, (b) air (oxygen), (c) light. There is strong evidence that the "peroxide catalyzed" isomerization is brought about by a bromine atom mechanism. Isostilbene was prepared free from peroxide and this pure isostilbene dissolved in benzene did not undergo isomerization in the dark in the presence of hydrogen bromide (Table 2, sec. c). The transformation was practically negligible when the reactants were mixed either in air or in a highly evacuated tube in the presence of antioxidants (e.g., hydroquinone, thiophenol, ethylmercaptan). However, the addition of a peroxidic substance (e.g., benzoyl peroxide, ascaridole) to the reaction mixture caused complete isomerization to stilbene in a few minutes. The time for complete isomerization varied with the amount of peroxide used, but even minute traces of peroxides caused complete conversion in thirty minutes. (Table 2, sec. e.) In direct sunlight or in artificial light, isostilbene, dissolved in benzene, is transformed into stilbene by hydrogen bromide in about five minutes. (Table 2, sec. a.) Here evacuation of the reaction vessel had a pronounced effect, in that twenty minutes were required for complete isomerization. (Table 2, sec. b.) Most striking, however, is the effect of antioxidants. Thus, hydroquinone, ethylmercaptan, etc., so retard the isomerization of isostilbene in benzene solution by hydrogen bromide that no stilbene can be found even after thirty minutes. (Table 2, sec. e.)

The effect of light is most interesting and the question arises whether it is the direct action of the light per se on the system (unsaturated hydrocarbon-halogen acid), or whether the minute trace of oxygen plays an essential role. Consistent with the last possibility is the fact that in all experiments where antioxidants were used light was not effective in causing

TABLE 2

ISOMERIZATION OF ISOSTILBENE TO STILBENE IN
BENZENE SOLUTION BY HYDROGEN BROMIDE

Section a In Air and Daylight			
No.	Moles of HBr per Mole of Isostilbene	Reaction Time	Final Products
1	1.0	2 minutes	Isostilbene (recovered)
2	1.0	5 "	Stilbene
3	1.0	10 "	Stilbene
4	1.0	10 "	Stilbene (duplicate of No. 3)
5	1.0	15 "	Stilbene
6	1.0	20 "	Stilbene
7	1.0	90 "	Stilbene and stilbene dibromide
8	1.0	19 hours	Stilbene and addition product
9	1.0	22.5 "	Stilbene and addition product

Section b In Vacuo and Sunlight ^a			
No.	Moles of HBr per Mole of Isostilbene	Reaction Time in Minutes	Final Products
10	1.5	10	Isostilbene and stilbene dibromide ^b
11	1.0	13	Isostilbene and stilbene
12	1.37	15	Isostilbene and stilbene
13	1.46	20	Stilbene
14	1.0	90	Stilbene

^aBenzene-hydrogen bromide solution was distilled into the isostilbene reaction vessel in vacuo (Kharasch-Mayo technique).

^bStilbene dibromide was formed as a by-product by the action of bromine liberated from the HBr by the action of light.

Section c In Air and Darkness			
No.	Moles of HBr per Mole of Isostilbene	Reaction Time in Minutes	Final Products
15	1.37	15	Isostilbene (recovered)
16 ^a	1.37	15	"
17	1.46	20	"
18 ^a	1.46	20	"
19 ^a	1.50	90	"
20 ^a	1.50	90	"
21 ^a	1.00	120	"

^aBenzene-hydrogen bromide solution was distilled into the isostilbene reaction vessel in vacuo. Then the reaction mixture was exposed to air for the stated interval.

TABLE 2--Continued

Section d In <u>Vacuo</u> and Darkness ^a			
No.	Moles of HBr per Mole of Isostilbene	Reaction Time in Minutes	Final Products
22	1.0	90	Isostilbene
23	1.5	90	"
24 ^b	1.5	30	"
25 ^c	1.5	15	"

^a Benzene-hydrogen bromide solution was distilled into the isostilbene reaction vessel in vacuo.

^b 0.036 millimoles of bromine present in reaction mixture.

^c Dioxane used as solvent instead of benzene.

Section e					
No.	Moles of HBr per Mole of Isostilbene	Type of Experiment	Reaction Time in Minutes	Peroxide or Antioxidant	Final Products
26	1.5	<u>Vacuo</u> , darkness	30	Ascaridole (one drop)	Stilbene
27	1.5	Air, darkness	30	Benzoyl Peroxide (0.02 g.)	Stilbene
28	1.5	<u>Vacuo</u> , sunlight	20	Ethyl Mercaptan (0.5 g.)	Isostilbene
29	1.5	<u>Vacuo</u> , 100 Watt Lamp	30	Hydroquinone (0.025 g.)	Isostilbene

isomerization.

The action of hydrogen chloride on isostilbene dissolved in benzene is very interesting. Isomerization is exceedingly slow, even in air, light and with added peroxides (see Table 3). Isostilbene dissolved in benzene was isomerized by five mole equivalents of hydrogen chloride only after standing for six days. It is interesting to note that the benzene solution went through a series of color changes during this interval (green-blue-violet). In an exactly similar experiment in which glacial acetic acid was used as a solvent there was no isomerization after six days. No color changes were observed in this experiment. It appears that with hydrogen chloride, we have an en-

tirely different reaction mechanism from that found with hydrogen bromide. The order of the reaction velocity is entirely different from the hydrogen bromide "peroxide catalyzed" reaction (isomerization in less than two minutes). We have therefore two reaction mechanisms which may be effective in isomerization, a fast one and a slow one. This point will be discussed later in greater detail under the topic of the isomerization of α -phenylcinnamic acid (labile) to α -phenylcinnamic acid (stable). As mentioned previously the mechanism of the "peroxide catalyzed" reaction is probably bromine atom catalyzed. Bromine atoms would be produced by the action of oxygen, or a peroxide, or by light on hydrogen bromide in the presence of oxygen. Once produced, they would convert isostilbene to stilbene by a chain reaction.

TABLE 3

THE ACTION OF HYDROGEN CHLORIDE ON ISOSTILBENE
IN VARIOUS SOLVENTS IN AIR

No.	Moles of HCl per Mole of Isostilbene	Solvent	Peroxide	Light	Reaction Time	Product
1	1.0	Benzene	None	Daylight	20 min.	Isostilbene (recovered)
2	1.0	Benzene	"	Daylight	17 hrs.	"
3	3.0	Ligroin	"	Daylight	22.5 hrs.	"
4	3.0	Benzene	"	100 W Lamp	8 hrs.	"
5	2.0	Benzene	Ascaridole (one drop)	100 W Lamp	30 min.	"
6	2.0	Benzene	"	Dark	30 min.	"
7	5.0	Acetic Acid	None	Dark	6 days	"
8	5.0	Benzene	"	Dark	6 days	Stilbene

It is well established by the work of Kharasch and his students that the most characteristic and striking difference between hydrogen chloride and hydrogen bromide is that the latter in the presence of oxygen and/or peroxides may function in an entirely different manner from hydrogen chloride. Hence those reactions in which hydrogen chloride and hydrogen bromide are equally effective are in a class by themselves. Reactions of this type are not catalyzed by peroxides. As an example of such a reaction, we may cite the isomerization of maleic acid to fumaric

acid, and the isomerization of dimethyl maleate to dimethyl fumarate. Experiments with these substances have proved that hydrogen chloride and hydrogen bromide are equally effective in causing isomerization, and hence the mechanism involved in their isomerization is neither catalyzed by peroxides nor bromine atoms.

b. Maleic Acid

Maleic acid was very readily isomerized to fumaric acid by halogen acids (hydrogen chloride and hydrogen bromide) in various solvents such as acetic acid, dioxane, and water (see Table 4). The isomerization was rather slow when dilute acid was used. However, concentrated acids converted the maleic acid completely to fumaric acid at room temperature in a short time. There appeared to be no definite peroxide effect since both hydrogen chloride and hydrogen bromide were equally effective as isomerizing agents; furthermore peroxides and antioxidants did not change the course of the reaction or appreciably influence the speed of the isomerization. No addition of halogen acids to maleic acid was ever observed in the experiments recorded in Table 4.

c. Dimethyl Maleate

The isomerization of dimethyl maleate occurred very readily in benzene solution in the presence of halogen acids. In oxygen-free experiments both with and without added antioxidants isomerization occurred in a short time. There was no decided difference in the air or vacuum experiments. (See Table 5.)

It appears therefore that there are two general types of substances, namely (1) unsaturated hydrocarbons, (2) unsaturated α - β -acids and esters which must be considered. The unsaturated hydrocarbon type of molecule as exemplified by isostilbene was rapidly isomerized by hydrogen bromide in the presence of peroxides, and slowly by hydrogen chloride. Unsaturated α - β -acids such as maleic acid and unsaturated esters such as dimethyl maleate were isomerized by hydrogen chloride or hydrogen bromide with equal facility.

d. α -Phenylcinnamic Acid

It was also decided to investigate the transformation of α -phenylcinnamic acid. It was found that in the dark the labile

TABLE 4

THE ISOMERIZATION OF MALEIC ACID TO FUMARIC ACID
BY HALOGEN ACIDS IN VARIOUS SOLVENTS

No.	Maleic Acid in Gms.	Reagent	Solvent ^a	Type of Exp.	Light	Reaction Time	Product (Acids)
1	1.0	HBr(sat.)	Acetic acid	Air	Diffused	Rapid	Fumaric
2	1.0	HCl(sat.)	Acetic acid	Air	Diffused	Rapid	Fumaric
3 ^b	1.0	HBr(sat.)	Acetic acid	Air	Diffused	Rapid	Fumaric
4	5.0	HBr(sat.)	Acetic acid	Vac.	Dark	1 hr.	Fumaric
5	1.2	HBr 2 mol eq.	Water	Air	Dark	8 wks.	Fumaric
6	1.2	HCl 2 mol eq.	Water	Air	Dark	8 wks.	Fumaric
7	1.7	HBr mol eq.	Water	Air	Dark	8 wks.	Fumaric
8	1.7	HCl mol eq.	Water	Air	Dark	8 wks.	Fumaric
9	1.2	None (control)	Water	Air	Dark	8 wks.	Maleic (recovered)
10	1.2	HBr 2 mol eq.	Dioxane	Vac.	Dark	15.5 hrs.	Fumaric (75% yield)
11	1.0	HBr(sat.)	Dioxane	Air	Diffused	10 min.	Fumaric
12 ^c	1.0	HBr(sat.)	Dioxane	Air	Diffused	<2 min.	Fumaric
13	1.0	HBr	Dioxane	Air	Sunlight	Rapid	Fumaric
14	1.0	HCl	Dioxane	Air	Diffused	Rapid	Fumaric

^aAbout 10 to 15 cc. of solvent was used for each experiment.

^bHydroquinone added (0.01 g.)

^cBenzoyl peroxide added (0.01 g.)

TABLE 5

THE ISOMERIZATION OF DIMETHYL MALEATE TO DIMETHYL
FUMARATE BY HALOGEN ACIDS IN BENZENE SOLUTION^a

No.	Dimethyl Maleate in Gms.	Halogen Acid	Type of Exp.	Peroxide or Antioxidant	Reaction Time	Product
1	1.0	HBr 1 mol eq.	Air		10 min.	Dimethyl fumarate
2	0.5	HBr 1.5 mol eq.	Vacuo		30 min.	"
3	0.5	HBr 1.5 mol eq.	Vacuo	Ethyl mercaptan	17 hrs.	"
4	0.5	HCl 1.0 mol eq.	Air		120 min.	"
5	0.5	HCl 1.5 mol eq.	Air		1 hr.	"

^aAbout 10-15 cc. of solvent was used for each experiment.

form of α -phenylcinnamic acid was isomerized by hydrogen bromide and a trace of peroxide (e.g., ascaridole, benzoyl peroxide) in less than two minutes (Table 6); in the dark hydrogen bromide in air required at least twenty minutes for isomerization; and with hydrogen bromide in the dark and in vacuo no isomerization occurred even after one hour. However, hydrogen bromide alone or even in the presence of antioxidants (e.g., hydroquinone, ethyl mercaptan) caused isomerization on standing for two to three days. In other words the peroxide catalyzed mechanism is quite rapid (less than two minutes) whereas the non-peroxide catalyzed mechanism is slow (two to three days). To prove that the non-peroxide catalyzed mechanism is the slow one, and that it will take place in the absence of peroxide it was necessary to show that hydrogen chloride is also effective in causing the isomerization, albeit slowly. The isomerization of the labile form of α -phenylcinnamic acid was found to occur after eleven days with hydrogen chloride, thus proving that the non-peroxide mechanism of isomerization with hydrogen chloride is slow but will actually occur on long standing.

e. Bromomaleic Acid

The addition of hydrogen bromide to bromomaleic acid was carried out in dioxane, ether, nitromethane, and water. Although light had no noticeable influence on the reaction, all additions were carried out in the dark. The products of the reaction depended on the amount of hydrogen bromide used and the length of time the substance was subjected to the action of the hydrogen bromide. If less than one mole equivalent of hydrogen bromide per mole of bromomaleic acid was used, in dioxane as a solvent, after a short time a small amount of meso-dibromosuccinic acid was found with unreacted bromomaleic acid after standing a short while. However on longer standing appreciable amounts of bromofumaric acid were also found (see Table 7, sec. a).

When an excess of hydrogen bromide was used (1-3 mole equivalents) and when the hydrogen bromide solution was relatively concentrated, addition occurred rapidly and completely; the product was meso-dibromosuccinic acid (up to 95% yield). A careful search was made for the racemic-dibromosuccinic acid but none was isolated. In the case where aqueous fuming hydrogen bromide was used likewise, no racemic-dibromosuccinic acid was formed in any

TABLE 6

THE ISOMERIZATION OF α -PHENYLGINNAMIC ACID (LABILE) TO
 α -PHENYLGINNAMIC ACID (STABLE) IN BENZENE SOLUTION BY
 HALOGEN ACIDS (0.5 GM. SAMPLES)

No.	Reagent (in mol eq's)	Type of Exp.	Peroxide or Antioxidant	Reaction Time	Result
1	HBr, 1.0	Air, darkness		5 min.	No isomerization
2	HBr, 1.0	" "		20 min.	"
3	HBr, 1.0	" "		25 min.	Isomerization
4	HBr, 1.0	" "		40 min.	"
5	HBr, 1.0	" "		1.0 hr.	"
6	HBr, 1.0	" "		1.0 hr.	" (dupli- cate of No. 5)
7	HBr, 1.0	" , 200 watt light		20 min.	Isomerization
8	HBr, 1.0	" "		60 min.	"
9	HBr, 1.0	" , daylight	Ascaridole 0.02 g.	<2 min.	"
10	HBr, 1.0	" "	Hydroquinone 0.02 g.	30 min.	No isomerization
11	HBr, 1.5	Vacuo, darkness		1.0 hr.	"
12	HBr, 1.5	" "		68 hrs.	Isomerization
13	HBr, 1.5	" "		15 min.	"
14	HBr, 1.5	" "	Benzoyl peroxide 0.02 g.	44 hrs.	"
15	HBr, 2.0	" "	Hydroquinone 0.03 g.	48 hrs.	"
16 ^a	HBr, 1.5	" "	Hydroquinone 0.04 g.	40 min.	No isomerization
17	HCl, 1.0	Air, darkness ^b		5 min.	"
18	HCl, 1.0	Air, daylight		15 min.	"
19	HCl, 1.0	" "		30 min.	"
20	HCl, 1.0	" "		3.5 hrs.	"
21	HCl, 1.0	" "	Ascaridole 0.02 g.	1.0 hr.	"
22	HCl, 3.0	" , darkness		48.5 hrs.	"
23	HCl, 5.0	" , daylight		11 days	Isomerization
24	HBr, 2.0	Vacuo, darkness	Ethyl mercaptan 0.1 g.	47 hrs.	"

^a The solvent used in this experiment was dioxane.

^b About 10-20 cc. of benzene solution was used.

appreciable amount. (See Table 7, secs. c and e.) Added peroxide (ascaridole) did not produce a noticeable change in either the rate of the reaction or in the course of the reaction. Antioxidants (SO_2 , hydroquinone) likewise did not produce any change in the products of the reaction.

f. Bromofumaric Acid

The addition of hydrogen bromide to bromofumaric acid was also carried out in various solvents, dioxane, ether, and water. In all solvents the rate of addition of hydrogen bromide to bromofumaric acid was considerably slower than the rate of addition of hydrogen bromide to bromomaleic acid. When less than one mole equivalent of hydrogen bromide in dioxane solution was used no addition occurred in fifteen minutes and even after sixty-five hours very little addition had occurred. However, when excess hydrogen bromide was used addition was quite appreciable in dioxane and ether. In these solvents both meso-dibromosuccinic acid (58%) and dl-dibromosuccinic acid (22%) were formed after the reaction proceeded for seven days.

Bromofumaric acid in fuming aqueous hydrogen bromide gave on standing for nineteen days meso-dibromosuccinic acid and a little dl-dibromosuccinic acid. However, more than half of the original bromofumaric acid was recovered (see Table 7, sec. e), indicating the extreme slowness of this reaction. This slowness of reaction was probably due to a large extent to the insolubility of the bromofumaric acid in the fuming hydrogen bromide solution.

g. The Action of Hydrogen Bromide on Racemic-Dibromosuccinic Acid

The racemic-dibromosuccinic acid when treated with hydrogen bromide under conditions similar to the addition reaction experiments, failed to be converted to the meso form (Table 8). It must therefore be concluded that the meso-dibromosuccinic acid was formed from the starting substance by direct addition of hydrogen bromide. In all the experiments with bromomaleic acid and hydrogen bromide in dioxane no evidence was obtained that isomerization occurred previous to addition. The addition likewise appeared to occur exclusively in a "trans manner," since only meso-dibromosuccinic acid was found in the final product.

TABLE 7

Section a
Addition of 1/2 Mole Equivalent of Hydrogen Bromide
in Dioxane to Bromomaleic Acid

No.	Bromomaleic Acid-gms.	Dioxane (in ml.)	Reaction Time	Products
1	1.0	10	15 min.	0.1 g. meso-dibromosuccinic acid 0.7 g. bromomaleic acid
2 ^a	1.0	10	15 min.	0.16 g. meso-dibromosuccinic 0.3 g. bromomaleic acid
3	1.0	5	40 min.	0.035 g. meso-dibromosuccinic 0.43 g. bromofumaric acid
4 ^b	1.0	10	40 min.	0.01 g. meso-dibromosuccinic 1.0 g. bromomaleic acid
5	1.25	10	4 hrs.	0.7 g. meso-dibromosuccinic 0.5 g. bromofumaric acid
6	1.0	10	60 hrs.	0.2 g. meso-dibromosuccinic 0.5 g. bromofumaric acid

^a0.01 g. of ascaridole was added to reaction mixture.

^bIn this experiment unpurified dioxane was used.

Section b
The addition of 1/2 Mole Equivalent of Hydrogen Bromide
in Dioxane to Bromofumaric Acid

No.	Bromofumaric Acid-gms.	Dioxane (in ml.)	Reaction Time	Products
1	1.0	10	15 min.	0.815 g. bromofumaric acid (re- covered)
2	1.0	5	18 hrs.	0.48 g. bromofumaric acid (re- covered)
3	1.0	5	65 hrs.	Trace meso-dibromosuccinic acid 0.68 g. bromofumaric acid (re- covered) 0.07 g. meso-dibromosuccinic acid

TABLE 7--Continued

Section c

The Addition of Hydrogen Bromide to Bromaleic Acid in Dioxane

No.	Bromaleic Acid-gms.	HBr (mol eq.)	Dioxane (in ml.)	Reaction Time	Products
1	2.5	1.25	10.9	3 min. 12 min. 22 min. 32 min. 54 min. 66 min.	Meso-dibromosuccinic acid (only) " " " " " " " " (six equal aliquots)
2	2.0	1.25	50.0	15 min.	Total yield 91% Meso-dibromosuccinic acid (0.13 g.) 12.5 ml. aliquot
3 ^a	1.0	1.25	10.0	15 min. 12.5 hrs.	Bromaleic (0.14 g.) Meso-dibromosuccinic acid -- 12.5 ml. aliquot
4	5.0	1.25	20.0	24 days	Meso-dibromosuccinic acid (1.37 g.) 25 ml. aliquot
5 ^b	1.0	1.25	50.0	15 min. 18 hrs.	Meso-dibromosuccinic acid (only) 5 ml. aliquot " " Meso-dibromosuccinic acid (only) 5 ml. " Total yield 95%
6	2.0	2.00	10.0	15 min. 6 hrs. 1 hr. 64 hrs.	Meso-dibromosuccinic acid (only) 25 ml. aliquot Meso-dibromosuccinic acid (only) Total yield 0.07 g. Meso-dibromosuccinic acid 0.105 g. Bromofumaric acid 0.072 g. 2.5 ml. aliquot Meso-dibromosuccinic acid 0.80 g. 7.5 ml. aliquot

-22-

^aSulfur dioxide passed into reaction mixture.^b50 mol% hydroquinone added to reaction mixture.

TABLE 7--Continued

-23-

Section d
The Addition of Hydrogen Bromide to Bromofumaric Acid in Dioxane

No.	Bromofumaric Acid-gms.	HBr (mol. eq.)	Dioxane (in ml.)	Reaction Time	Products
1	1.0	2.0	5.0	60 hrs.	Meso-dibromosuccinic acid 0.56 g.
2	2.0	2.0	10.0	63.5 hrs.	Meso-dibromosuccinic acid 0.36 g. Bromofumaric acid 0.50 g.
3	1.0	3.0	10.0	5 days	Meso-dibromosuccinic acid 0.725 g.--51% Racemic-dibromosuccinic acid 0.09 g.--6.3%
4 ^a	2.0	2.0	20.0	5 days	Oily residue 0.92 g. Meso-dibromosuccinic acid 1.53 g. Racemic-dibromosuccinic acid 0.76 g.
5	1.0	1.25	10.0	7 days	Meso-dibromosuccinic acid 0.825 g.--58% Racemic-dibromosuccinic acid 0.315 g.--22%

^aEther used as solvent in experiment 4.

Section e
The Addition of Hydrogen Bromide to Bromomaleic and Bromofumaric Acids in Water (Saturated with HBr at -10° C.)

No.	Acid in Gms.	Water (in ml.)	Reaction Time	Products
1	6.0 bromomaleic	30.0	44 hrs.	Meso-dibromosuccinic acid 4.0 g. Racemic-dibromosuccinic acid 0.96 g.
2	2.0 bromomaleic	5.0	12 hrs.	Meso-dibromosuccinic acid Racemic-dibromosuccinic acid
3	3.0 bromomaleic	15.0	6 hrs.	Meso-dibromosuccinic acid
4	6.0 bromofumaric	25.0	11 days	Meso-dibromosuccinic acid (trace) Bromofumaric acid (recovered) 3.5 g.
			19 days	Racemic-dibromosuccinic 0.1 g.

TABLE 7--Continued

Section f The Addition of Halogen Acids to Bromomaleic Acid in Various Solvents				
No.	Acid	Solvent ^a	Reaction Time	Product
1	HBr (sat.)	Ether	5 min.	Meso-dibromosuccinic acid
2	HBr (sat.)	Ether	20 min.	Meso-dibromosuccinic acid
3	HBr (sat.)	Ether	60 min.	Meso-dibromosuccinic acid
4	HCl (sat.)	Ether	3.5 hrs.	Chlorobromosuccinic acid
5	HCl (sat.)	Ether	Overnight	Chlorobromosuccinic acid
6	HCl, 1/2 mol eq.	Water	37 hrs.	Bromofumaric acid--50% yield
7	1:1, HCl	Water	5 min. (boiled)	Bromomaleic acid (recovered)
8	HCl (sat.)	Water	1.5 hrs.	Bromomaleic acid (recovered)
9	HBr, 1.5 mol eq.	Nitro- methane	12 hrs.	Meso-dibromosuccinic acid--60% yield
10	HBr, 3 mol eq.	Nitro- methane + ether	12 hrs.	Meso-dibromosuccinic acid--95% yield
11	HBr, 3 mol eq.	Nitro- methane	16 hrs. (in vacuo)	Meso-dibromosuccinic acid--83% yield

^a About 10 to 20 cc. of solvent was used in these experiments.

TABLE 8

EXPERIMENTS TO DETERMINE WHETHER RACEMIC-DIBROMOSUCCINIC
ACID IS ISOMERIZED BY HYDROGEN BROMIDE; IN
SOLUTION, IN AIR, AND IN DIFFUSED LIGHT

No.	Grams of Acid	HBr (mol eq's)	Solvent	Reaction Time	Result
1	2.00	1.25	20 ml. Dioxane	7 days	Racemic-dibromosuccinic acid recovered 88% of original
2	1.00	1.25	10 ml. Dioxane	7 days	Racemic-dibromosuccinic acid recovered 83% of original
3	1.00	1.25	10 ml. Ether	7 days	Racemic-dibromosuccinic acid recovered 98% of original

However, with bromofumaric acid, although the meso-dibromosuccinic acid was formed to the extent of over 80%, definite yields in favorable cases, even as high as 22% of the racemic-dibromosuccinic acid, were obtained. Now, from bromofumaric acid, the mesodibromosuccinic acid can be formed only by a "cis addition" to the double bond; and the racemic-dibromosuccinic acid can be formed only by a "trans addition" to the double bond. It appears, however, as though the "trans addition" to the malenoid compound in dioxane (bromomaleic acid) is so much more rapid than the "cis addition" that, if any, only undetectable traces of the racemic-dibromosuccinic acid is formed. In water, the "trans addition" to bromomaleic acid is not quite so rapid, and this permits the slower "cis addition" to occur, thus yielding small amounts of the racemic along with the meso-dibromosuccinic acid. As shown by the experimental results in the case of bromofumaric acid, the addition of hydrogen bromide in dioxane solution is slow, and here we get, as mentioned above, both the racemic and the meso forms of addition products.

h. Chlormaleic Acid

The addition of hydrogen chloride to chloromaleic acid in dioxane was very slow. It was found that no isomerization occurred previous to addition. After two days, it was possible to recover unchanged almost all the chloromaleic acid in experiments in which chloromaleic acid dissolved in dioxane was treated with two or three mole equivalents of hydrogen chloride. On longer standing, however, addition did take place. After seven days it was found that addition occurred to the extent of 93% on the basis of the neutralization equivalent of the final product.

i. Citraconic and Mesaconic Acids

In many respects, the addition of hydrogen bromide to citraconic acid (cis) was similar to the addition of hydrogen bromide to bromomaleic acid. As in the case of bromomaleic acid, hydrogen bromide in dioxane solution added very readily to citraconic acid, giving as high as 97% addition product, namely, citra-bromopyrotartaric acid. Added peroxide produced no noticeable effect on the course or rate of the addition of hydrogen bromide to citraconic acid. (See Table 9.) The addition apparently oc-

TABLE 9

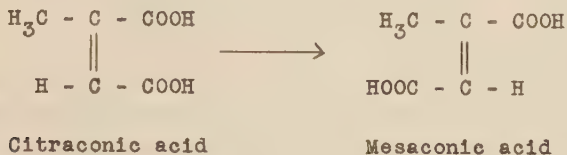
THE ADDITION OF HYDROGEN BROMIDE TO CITRAGONIC
AND MESACONIC ACIDS IN DIOXANE SOLUTION

No.	Acid Present (Ethyleneic)	HBr (mol eq's)	Dioxane (in ml.)	Reaction Time	Products Formed (Acids)
1	Citraconic, 1.0 g.	1.5	10	1 hr.	Citrabromopyrotartaric--97% addition
2	"	"	"	7 days	"
3 ^a	"	"	"	10 min.	"
4	"	0.16	"	3 days	"
5 ^b	"	1.5	"	3 days	Mesaconic--0.2 g. Citrabromopyrotartaric--0.05 g. Unknown residue--0.6 g.
6	"	1.0	50	3 hrs.	Citrabromopyrotartaric--0.59 g. Unknown residue--1.07 g. Citrabromopyrotartaric--0.62 g. 95% addition
7	Mesaconic, 1.0 g.	1.5	10	2.5 hrs.	Mesaconic acid recovered--0.15 g. Citrabromopyrotartaric--0.2 g.
8	"	1.5	10	10 min.	Mesaconic acid recovered--0.85 g.

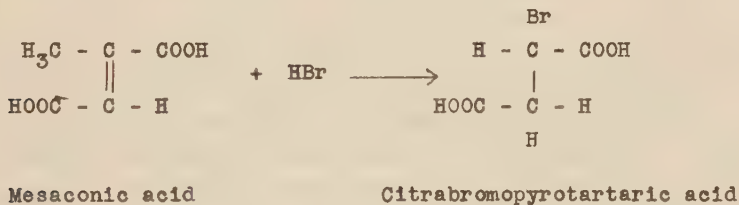
^a Benzoyl peroxide (0.01 g.) was added to the reaction mixture.

^b Ascaridole (0.07 g.) was added to the reaction mixture.

curred directly to the malenoid form (citraconic acid). Isomerization occurred previous to addition only when less than a mole equivalent of halogen acid was employed (Table 9).



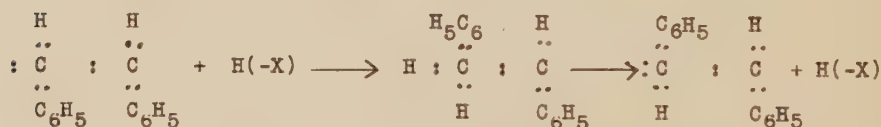
The addition of hydrogen bromide to mesaconic acid (trans) required a much longer time than the addition of hydrogen bromide to citraconic acid. This is supporting evidence that the addition of the halogen acid takes place directly to the malenoid form. As in the case of citraconic acid, the addition product was the normal addition product, namely, citrabromopyrotartaric acid.



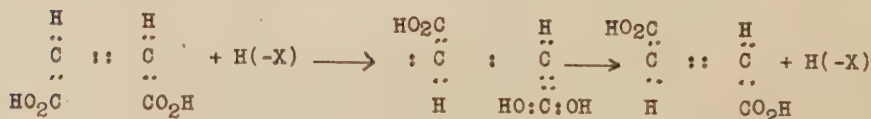
PROPOSED MECHANISMS FOR THE ISOMERIZATION
OF CIS TO TRANS COMPOUNDS

The results discussed thus far indicate that there are two mechanisms by which cis ethylenic derivatives may be isomerized into the corresponding trans isomers: (1) a reaction in which hydrogen chloride is approximately as effective as hydrogen bromide, and (2) a reaction in which hydrogen bromide and oxygen or a peroxide is effective, but in which hydrogen chloride is not.

The first reaction has been known for many years and, from the fact that the reaction is common to several strong acids, it shall be designated as the "ionic" mechanism without specifying definitely whether the ionized fragments or the unionized acid is responsible for the conversion. In general, the isomerization is very slow in the case of isostiblene, very fast in the case of maleic and dimethyl maleate, and of intermediate velocity in the case of labile α -phenylcinnamic acid. This reaction is best interpreted as an addition of a proton (the data do not allow differentiation between a "proton" catalyzed reaction and a negative ion catalyzed reaction) to one of the carbon atoms of the ethylenic bond as indicated by the highly schematic formulas below, free rotation and inversion of the groups about the other carbon atom, and finally loss of a proton:

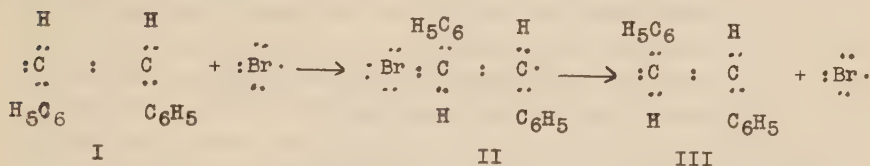


In the case of molecules in which a carbonyl group is conjugated with the ethylenic bond, the proton may add to the carbonyl group instead of to the ethylenic bond;



The experimental results indicate clearly that the isomerization is much more rapid with such compounds than with hydrocarbons.

The peroxide catalyzed isomerization reaction has been observed with hydrogen bromide in the presence of oxygen, peroxides, or light. It shall be designated as the "bromine-atom" mechanism. The peroxide effect in the addition of hydrogen bromide to unsaturated compounds has been interpreted³⁸ on the basis that hydrogen bromide and oxygen or peroxides react to form bromine atoms which act as chain carriers for the addition reaction. Since the same conditions lead to the rapid isomerization of isostilbene to stilbene, it was natural to extend the "atom-mechanism" to include isomerization as well as addition reactions.³⁹ The schematic diagrams below indicate how a bromine atom may cause such an isomerization to take place:



The free radical II loses a bromine atom unless the concentration of hydrogen bromide is high enough so that the chain mechanism for the addition reaction indicated above can operate efficiently. It is noteworthy that a peroxide effect was observed in the isomerization of isostilbene and the labile α -phenylcinnamic acid, which are isomerized relatively slowly in the absence of peroxides, but not in the case of maleic and bromomaleic acids, which are relatively rapidly isomerized by halogen acids.

³⁸Kharasch, Engelmann and Mayo, J. Org. Chem., **2**, 288 (1937).

³⁹Kharasch, Mansfield and Mayo, J. Am. Chem. Soc., **59**, 1155 (1937).

EXPERIMENTAL PART

Materials Used

Benzene (thiophene free Merck Reagent) was dried over sodium wire and then distilled. Dioxane was purified by the procedure of Eigenberger:⁴⁰ Crude dioxane was refluxed on the steam bath for seven hours with 10% of its weight of normal aqueous hydrochloric acid. A slow stream of air was simultaneously passed through the solution to eliminate the acetaldehyde formed by the decomposition of ethylene acetal, which is the main impurity in dioxane. The solution was then treated with solid sodium hydroxide and after separation of the aqueous layer, again kept over sodium hydroxide pellets for one day. Finally, the dioxane was distilled from sodium wire. The purified dioxane still gave a negative test for peroxides after standing for six months in a dark bottle. The peroxide test was performed by adding a few cc. of 10% potassium thiocyanate to a few crystals of ferrous ammonium sulfate and then adding a few drops of the dioxane.

Nitromethane was prepared according to the directions outlined in "Organic Syntheses."⁴¹

Ether used in this work was anhydrous Mallinckrodt Analytical Reagent quality.

Hydrogen bromide was generated by the action of bromine on hot tetralin in a specially designed apparatus which has been used for a number of years in this laboratory. The hydrogen bromide was purified by passing it through a calcium chloride tube and then a tube packed with naphthalene. In some of the early experiments, the hydrogen bromide was purified by passing it through a train consisting of a calcium chloride tube, a tube immersed in a carbon dioxide-acetone bath, and finally a tube containing a tightly wound copper spiral. When it was discovered that a bromine-free hydrogen bromide could be prepared by the first method described, the latter, more complicated train was

⁴⁰Eigenberger, J. prakt. Chem., **130**, 78 (1931).

⁴¹"Organic Syntheses," Vol. III, John Wiley and Sons, Inc., New York, 1923, p. 83.

discarded in favor of the simpler one.

Hydrogen chloride was generated by the action of concentrated sulfuric acid on concentrated hydrochloric acid.

Preparation of Compounds

Isostilbene.--This compound was prepared in 75% yield by modifying the method of Taylor and Crawford.⁴² They report a 65% yield. The method consists in decarboxylating α -phenylcinnamic acid (stable)⁴³ in quinoline solution, using copper chromite⁴⁴ as catalyst. A mixture of α -phenylcinnamic acid (stable) (24.3 g.), quinoline (212 cc.), and copper chromite (2 g.) was heated to 220-30° for one hour and twenty minutes, in a 500 cc. round-bottomed flask to which an air reflux condenser was attached. Upon cooling, the mixture was poured into sufficient dilute hydrochloric acid to combine completely with the quinoline. The solution was then extracted with ether. The ether was evaporated, after which the residue was dissolved in petroleum ether and cooled to 0°, and filtered. (Stilbene, which is insoluble in cold petroleum ether, is thus separated from the product.) After distilling off the petroleum ether, the crude isostilbene was successively treated in a separatory funnel with dilute sodium carbonate solution, 5N sulfuric acid solution, and finally washed with water. It was then distilled through a fractionating column, under reduced pressure. There was obtained 14.7 g. of pure isostilbene, b_7 128-9°.

α -Phenylcinnamic acid.--In a 1-liter round-bottomed flask, equipped with an extra long reflux condenser, there was placed a mixture of 180 g. (1.14 moles) of sodium α -toluate, 480 g. (4.71 moles) of acetic anhydride, and 120 g. (1.13 moles) of freshly distilled benzaldehyde (b.p. 177-8°). The air in the entire system was displaced by carbon dioxide, and the mixture heated on the steam bath for 72 hours. Upon cooling, water was added to decompose the excess acetic anhydride, and then sufficient aqueous sodium hydroxide was added to neutralize the acetic acid and render the solution slightly alkaline. The product was

⁴²Taylor and Crawford, J. Chem. Soc., 1130 (1934).

⁴³Bakunin, Gazz. Chem. Ital., 27 11, 49 (1897); 31 11, 77 (1901).

⁴⁴Adkins and Connor, J. Am. Chem. Soc., 53, 1092 (1931).

then steam distilled until all volatile substances were removed (benzaldehyde and stilbene), and the solution decolorized by boiling it with charcoal and filtering it through a steam funnel.

α -Phenylcinnamic acid (stable) was precipitated by adding drop by drop a dilute solution of acetic acid to the vigorously stirred solution. The yield of α -phenylcinnamic acid (stable), m.p. $172-3^{\circ}$, was 183 g. (71.4%). By adding hydrochloric acid to the filtrate from above, it was found possible to precipitate a small amount of α -phenylcinnamic acid (labile). The yield of α -phenylcinnamic acid (labile), m.p. $135-6^{\circ}$, was 11.2 g. (4.4%).

Dimethyl maleate.--This compound was prepared by the method of Clemo and Graham:⁴⁵ maleic anhydride (60 g.) was added to methyl alcohol (100 cc.) and concentrated sulfuric acid (4 cc.), and the mixture refluxed for three and a half hours on the water bath. The bulk of the excess alcohol was then distilled off and water added, followed by solid sodium carbonate to neutralize the sulfuric acid. The ester, when extracted with ether, dried over sodium sulfate and fractionated, gave: (a) 6 g., b.p. $200-4^{\circ}$; (b) 65 g., b.p. $204-6^{\circ}$; (c) 1-2 g., b.p. above 206° . Fraction (a) contained traces of methyl fumarate, as shown by the silver nitrate test after hydrolysis with baryta.

The methyl fumarate formed by the isomerization of the above was identified by melting point and by mixed melting point with an authentic specimen.

Bromomaleic acid.--This compound was prepared according to the method of Michael.⁴⁶ Twenty-five grams of dibromosuccinic acid was heated with 100 cc. of water under reflux for five hours. The solution was then evaporated almost to dryness on the steam bath. The residue was collected at the filter pump and washed with a small amount of water until the filtrate was colorless. The bromomaleic acid was then recrystallized from nitromethane. It was found that this recrystallization yielded an exceedingly pure crystalline product, m.p. $136-7^{\circ}$. Bromomaleic acid was also prepared according to the method of P. Walden:⁴⁷ fifty grams of dibromosuccinic acid was distilled with twenty-five grams of

⁴⁵Clemon and Graham, J. Chem. Soc., 215 (1930).

⁴⁶A. Michael, J. prakt. Chem., 52, 289 (1895); J. Am. Chem. Soc., 16, 188 (1894).

⁴⁷P. Walden, Ber., 30, 2886 (1897).

phosphorus pentoxide under atmospheric pressure, then redistilled with a little phosphorous pentoxide in vacuum. The bromomaleic anhydride was allowed to react with a small amount of water, to give twenty-five grams of bromomaleic acid.

Bromofumaric acid.--This compound was prepared according to the method of Michael.⁴⁸ Twenty-five grams of isodibromosuccinic acid and 75 cc. of water were heated under reflux for four hours. The solution was then evaporated on the steam bath, until about 25 cc. of solution remained, because bromofumaric acid is slightly soluble in mineral acids. The product was filtered and washed with a small amount of water. The bromofumaric acid was finally recrystallized from ethyl acetate. A pure product was obtained, m.p. 185-6°.

Dibromosuccinic acid.--This compound was prepared by the method of Eichelberger.⁴⁹ The method consisted of brominating an aqueous solution of sodium fumarate in the presence of a large amount of sodium bromide. Twenty-five grams of pure fumaric acid was placed in a 1-liter flask, 350 cc. of water was added and the acid neutralized to the pink point of phenolphthalein with approximately 75 cc. of 20% sodium hydroxide solution. Now, one hundred grams of powdered sodium bromide was added slowly during constant shaking. Fifteen cc. of bromine dissolved in 250 cc. of a 20% solution of sodium bromide was added slowly to the sodium fumarate mixture while the flask was rotated. The reaction mixture was allowed to stand thirty minutes and the excess bromine removed by addition of sodium bisulfite. Concentrated hydrochloric acid was added, and the dibromosuccinic acid was precipitated at once. The crystals were collected on a filter, washed with water and dried in a vacuum over sulfuric acid.

Dichlorosuccinic acid.--This compound was prepared by the method of Robinson and Lewis.⁵⁰ This method was a modification of the procedure suggested by Terry and Eichelberger.⁵¹

Isodibromosuccinic acid.--This compound was prepared by

⁴⁸A. Michael, J. prakt. Chem., 52, 301 (1895).

⁴⁹L. Eichelberger, J. Am. Chem. Soc., 48, 1321 (1926).

⁵⁰Robinson and Lewis, J. Chem. Soc., 1260 (1933).

⁵¹Terry and Eichelberger, J. Am. Chem. Soc., 47, 1067 (1925).

the procedure of McKenzie.⁵² Bromine (19 cc.) was gradually added within an interval of five minutes to 400 cc. of cool anhydrous ether. After ten minutes, the clear liquid began to become turbid, and at this stage the addition of maleic acid (40 g.) was started, about 2 g. being added each time with constant shaking.

The temperature was not allowed to rise above 25°. Very little hydrogen bromide was evolved at the end of the reaction, and a mere trace of fumaric acid was found. The preparation must be carried out in dull light. The orange-colored solution after being washed once with water, then with sulfurous acid, and finally twice with water, was dried over anhydrous sodium sulfate. The ether was then evaporated off at room temperature to avoid decomposing the bromo-acid and the residual oily solid was dried in vacuo over sulfuric acid. It was found that a very pure product could be readily obtained by recrystallizing the crude bromo-acid from nitromethane. The purified isodibromosuccinic acid melted at 170-171.5°, and the neutralization equivalent was 136.9.

Chloromaleic acid.--This compound was prepared by the method of van der Riet.⁵³ Dichlorosuccinic acid (4 g.), sodium acetate (4 g.), and water (50 cc.) were mixed and refluxed on the steam bath for four hours. The solution was then extracted with ether. The ether solution on evaporation gave a small amount of a mixture of chloromaleic and chlorofumaric acids. The aqueous solution was then strongly acidified with hydrochloric acid and again extracted with ether. On evaporation of the ethereal extract, there was obtained 2 g. of pure acid, m.p. 108°.

Maleic acid.--This compound was purified by converting it into the anhydride as follows: the acid was mixed with 70% of its weight of phosphorus pentoxide in a distilling flask. The mixture was melted, then vacuum distilled at 100-110°. The anhydride obtained was recrystallized from chloroform; final melting point 53°; yield 99%. The anhydride was treated with water and allowed to crystallize by concentration in vacuo. The product melted at 130-131°.

Fumaric acid.--This acid was readily obtained from pure maleic acid by boiling it with hydrochloric acid solution and

⁵² McKenzie, J. Chem. Soc., 101, 1200 (1912).

⁵³ Van der Riet, Ann., 280, 229 (1894).

recrystallizing the product from hot water. Samples dried in a vacuum over sulfuric acid were found to melt at 285° in a sealed tube.

Citraconic acid.--This compound was prepared according to the method outlined in "Organic Syntheses."⁵⁴ To 22.4 g. (0.2 mole) of pure citraconic anhydride in a 100 cc. beaker there was added from a pipette exactly 4 cc. (0.22 mole) of distilled water. The mixture was stirred on a hot plate until a homogeneous solution was formed, and then covered with a watch glass and allowed to stand for forty-eight hours. At the end of this time, it had completely solidified. The yield was 26 g., m.p. $87-9^{\circ}$. For further purification, it was finely ground in a mortar, washed with 50 cc. of cold benzene, dried in the air, and then dried for 24 hours in a vacuum desiccator over phosphorus pentoxide. The yield was 24.4 g. (94% of theory); m.p. $92-3^{\circ}$.

Citraconic anhydride.--This compound was prepared according to the method outlined in "Organic Syntheses."⁵⁵ Two hundred and fifty grams of itaconic anhydride was rapidly distilled at atmospheric pressure in a 500 cc. modified Claisen flask with a 15 cm. fractionating column. The receivers for the distillates were changed without interrupting the distillation. The distillate passing over below 200° consisted of water and other decomposition products. The fraction which distilled between $200-215^{\circ}$ consisted of citraconic anhydride, and was collected separately. The yield was 176-180 g. (68-72% of the theory), m.p. $5.5-6.0^{\circ}$. On redistillation under reduced pressure, there was obtained 155-165 g. (62-66%), b.p. $105-110^{\circ}$ at 22 mm., m.p. $7-8^{\circ}$.

Itaconic anhydride.--The preparation of this compound was carried out as suggested in "Organic Synthesis."⁵⁶ A 500 cc. Pyrex Kjeldahl flask was fitted with an outlet tube 12 mm. in diameter, bent downward for distillation. It was attached to a 100 cm. water-cooled condenser having an indented Pyrex inner tube. Two 250 cc. long-neck distilling flasks were used as receivers, the vapors being led to the center of each flask by means of an adapter and glass tubing. Both receivers were cooled in a mixture of ice and water.

⁵⁴"Organic Syntheses," Vol. XI, p. 28.

⁵⁵Ibid.

⁵⁶Ibid., p. 70.

Two hundred grams of citric acid (0.95 mole) was placed in the reaction flask and heated with a free flame until melted. Then the flask was heated very rapidly with a larger Meeker burner, and the distillation completed as rapidly as possible. The distillate was immediately poured into a separatory funnel, and the lower layer of itaconic anhydride separated. The yield of anhydride was 45 g. (38% of the theoretical).

General Procedure for the Reaction of Unsaturated Derivatives with Halogen Acid

The customary method of carrying out the air experiments was the following: in a glass stoppered vessel there was placed a weighed amount of the ethylenic derivative and then a solvent containing the requisite amount of halogen acid was added. The reaction was then allowed to proceed for the required time, and then the solvent and excess halogen acid were evaporated in vacuo over sulfuric acid and sodium hydroxide.

The vacuum experiments were carried out using the well-known technique of Kharasch and Mayo.⁵⁷

Separation and Identification of Reaction Products

Isostilbene.--The reaction product in the case of the isostilbene experiments was treated with hot alcohol, in which stilbene and isostilbene were soluble; the dibromostilbene (by-product from a side reaction), however, was insoluble in hot alcohol and was separated from the stilbene by filtration. Stilbene crystallized from the alcoholic solution on cooling. It was identified by its melting point and by a mixed melting point with an authentic specimen. The isostilbene was identified by converting it into stilbene by the action of alcoholic hydrogen bromide solution in the light. The stilbene thus formed was identified as indicated above.

α -Phenylcinnamic acid (labile).--The reaction product in the case of α -phenylcinnamic acid (labile) was treated with a hot alcohol-water solution, from which the original or the isomerized ethylenic derivative crystallized in a pure state. Identification was established by the melting point and by mixed melting point with an authentic specimen.

⁵⁷Kharasch and Mayo, J. Am. Chem. Soc., 55, 2468 (1933).

Maleic acid.--The reaction product in the case of the maleic acid experiments was always fumaric acid. The fumaric acid was identified by its melting point in a sealed tube, a mixed melting point with an authentic specimen, and by its neutralization equivalent.

Bromomaleic acid.--In the bromomaleic acid experiments, the final products were separated by the following procedure. A few tenths of a cc. of ice cold water was added to the product. This dissolved the unreacted bromomaleic acid and the racemic-dibromosuccinic acid. The meso-dibromosuccinic acid was collected at the filter pump and after recrystallization from hot water was identified by its melting point, mixed m.p. with an authentic specimen, and by its neutralization equivalent. The bromomaleic acid was identified after recrystallization from nitromethane by melting point, mixed m.p. with an authentic sample, and by its neutralization equivalent. The racemic-dibromosuccinic acid was identified after recrystallization from ethyl acetate by its m.p., mixed melting point, and neutralization equivalent.

Bromofumaric acid.--The products in the experiments with bromofumaric acid were separated and identified by the same procedure that was used in the bromomaleic acid experiments. The bromofumaric acid was identified after recrystallization from ethyl acetate by melting point, mixed melting point, and its neutralization equivalent.

Chloromaleic acid.--The procedure adopted for the separation and the identification of the products was similar to that used in the experiments with bromomaleic acid.

Citraconic acid, mesaconic acid.--The final reaction products were separated by taking advantage of the relative insolubility of mesaconic acid in cold water. Mesaconic acid, citraconic acid and the addition product formed from both by reaction with hydrogen bromide, namely citrabromopyrotartaric acid, were identified by melting point, mixed melting point, and finally by neutralization equivalent.

SUMMARY AND CONCLUSIONS

1. Isostilbene dissolved in benzene is isomerized very rapidly to stilbene by hydrogen bromide in the presence of (a) peroxides, (b) air (oxygen) and light, and (c) vacuo and light.

2. Isostilbene dissolved in benzene is not isomerized even after a long time by hydrogen bromide in air and darkness.

3. Isostilbene dissolved in benzene is not isomerized to stilbene even after a long time by hydrogen bromide in the presence of antioxidants.

4. Isostilbene dissolved in benzene is isomerized to stilbene by hydrogen chloride only after a very long time. The mechanism of this reaction is undoubtedly different from the rapid "peroxide catalyzed" reaction.

5. Isostilbene under antioxidant conditions adds hydrogen bromide more rapidly than does stilbene.

6. α -Phenylcinnamic acid (labile) is rapidly isomerized to α -phenylcinnamic acid (stable) by hydrogen bromide in the presence of (a) peroxides, (b) air (oxygen), (c) air and light.

7. α -Phenylcinnamic acid (labile) is slowly isomerized by hydrogen bromide in (a) vacuo and dark, (b) in the presence of antioxidants in either air or vacuo in the light.

8. α -Phenylcinnamic acid (labile) is very slowly isomerized to α -phenylcinnamic acid (stable) by hydrogen chloride.

9. Bromomaleic acid adds halogen acids very rapidly to give meso-dibromosuccinic acid. The addition probably occurs before the isomerization to the trans form.

10. Bromofumaric acid adds halogen acids more slowly than bromomaleic acid. Both meso-dibromosuccinic acid and racemic-dibromosuccinic acid are formed.

11. Maleic acid is rapidly converted to fumaric acid by both hydrogen bromide and hydrogen chloride in various solvents (dioxane, water, acetic acid).

12. Dimethyl maleate is rapidly isomerized by halogen acids in various solvents.

13. Citraconic acid adds halogen acids very rapidly to give citrabromopyrotartaric acid. The addition undoubtedly occurs before the isomerization can take place.

14. Citraconic acid is isomerized to mesaconic acid by hydrogen bromide in dioxane solution when insufficient hydrogen bromide is employed to combine completely with the citraconic acid. In similar experiments with bromomaleic acid, supporting, but not conclusive evidence was obtained that isomerization occurred previous to addition.

